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Caries experience in children with Marfan syndrome – a non-interventional case-control study**

Introduction: The Marfan syndrome is a rare connective tissue disorder with autosomal dominant inheritance. The aim of the present study was to evaluate the caries experience in children and adolescents with Marfan syndrome.

Materials and Methods: 31 children with Marfan syndrome (Marfan group; mean age: 8.77 ± 3.72 years) and 31 systemically healthy children (control group; mean age: 9.77 ± 3.72 years) were dentally examined according to WHO criteria. The recorded parameters included the dmft/DMFT (differentiated into dt/DT, mt/MT, ft/FT), the dmfs/DMFS (differentiated into ds/DS, ms/MS, fs/FS), the caries restoration index (CRI), and the hygiene index (HI). Statistical evaluation was carried out using t-test for independent samples and chi-square test ($p \leq 0.05$) using the statistics software program IBM SPSS Statistics 26.

Results: The children of the Marfan group had a significantly lower dmft ($p = 0.040$) and ft ($p = 0.040$) than children in the control group. There were no significant differences between the two groups when considering permanent dentition. However, the Marfan group tended to have a lower DMFT ($p = 0.064$), DT ($p = 0.076$) and FT ($p = 0.059$) than the control group. The HI was significantly higher in the control group than in the Marfan group ($p < 0.001$).

Conclusion: In the present study, children and adolescents with Marfan syndrome did not show a higher caries experience compared to a systemically healthy control group.

Keywords: Marfan syndrome; caries experience; children; adolescents; DMFT; DMFS

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Introduction

Marfan syndrome is a rare connective tissue disease with autosomal dominant inheritance [23]. The incidence of classic Marfan syndrome is reported in literature to be 2–3 per 10,000 inhabitants, regardless of gender or ethnicity [18]. Persons with Marfan syndrome usually have a large, lean stature, long extremities, arachnodactyly (Fig. 1), joint hypermobility, and deformities of the thorax and spine (e.g., scoliosis) [7]. More than 1000 different mutations in the fibrillin-1 (FBN1) gene on chromosome 15 have been identified as the cause of classical Marfan syndrome [26]. Since the clinical picture of Marfan syndrome is variable and the genetic causes are heterogeneous, it is difficult to distinguish it from other diseases of the connective tissue (e.g., Loeys-Dietz syndrome, Ehlers-Danlos syndrome, Shprintzen-Goldberg syndrome, Weill-Marchesani syndrome) [1]. For the diagnosis of Marfan syndrome, the use of the revised version of Ghent-nosology has proven to be of value. In addition to the detection of an FBN1 mutation and a family history, the manifestations of an aortic aneurysm and an ectopia lentis are taken into account [9, 22]. Cardiovascular complications such as aortic dilatation, dissection and rupture were the main reason why patients with Marfan syndrome had a reduced life expectancy compared to the normal population [24]. Although there is still no causal therapy available for Marfan syndrome, drug therapy and, in advanced cases, cardiovascular surgery have significantly increased life expectancy [19, 29].

Characteristic orofacial manifestations such as retrognathia, dolichocephaly, Gothic palate, cranio-mandibular dysfunctions and oligodontia or hypodontia have been described in people with Marfan syndrome [2, 8, 12]. An increased prevalence of pulp calcifications has also been demonstrated [3]. An increased incidence of periodontal disease is controversially discussed in literature, but could not be confirmed by our research group [30–32]. The dentition of patients with Marfan syndrome often shows crowded teeth, making

	Marfan	Control	Significance (p-value)
	n = 31	n = 31	
Age [years]	8.77 ± 3.72	9.77 ± 3.72	0.294*
HI [%]	75.36 ± 16.58	89.44 ± 8.59	< 0.001*
Permanent teeth	n = 29	n = 28	
DMFT	0.52 ± 1.64	1.57 ± 2.46	0.064*
DT	0.03 ± 0.19	0.36 ± 0.91	0.076*
MT	0.14 ± 0.74	0.00 ± 0.00	0.326*
FT	0.34 ± 1.05	1.25 ± 2.24	0.059*
DMFS	1.59 ± 6.70	2.61 ± 4.24	0.496*
DS	0.07 ± 0.37	0.46 ± 1.26	0.121*
MS	0.69 ± 3.71	0.00 ± 0.00	0.326*
FS	0.83 ± 3.08	2.18 ± 4.05	0.163*
DMFT = 0	n = 24	n = 15	0.018#
CRI (permanent teeth)	80.00 ± 44.72	76.26 ± 40.71	0.867*
Deciduous teeth	n = 22	n = 20	
dmft	0.41 ± 0.59	1.35 ± 1.84	0.040*
dt	0.23 ± 0.43	0.15 ± 0.49	0.077*
mt	0.00 ± 0.00	0.10 ± 0.45	0.330*
ft	0.18 ± 0.40	1.05 ± 1.73	0.040*
dmfs	0.77 ± 1.15	3.05 ± 4.92	0.056*
ds	0.41 ± 0.80	0.30 ± 0.98	0.693*
ms	0.00 ± 0.00	0.50 ± 2.24	0.330*
fs	0.36 ± 0.79	2.20 ± 4.10	0.063*
dmft = 0	n = 14	n = 10	0.372#
CRI (deciduous teeth)	43.75 ± 49.55	80.00 ± 42.16	0.113*

HI: hygiene index; dmft/DMFT: decayed missing filled teeth Index; dt/DT: decayed teeth; mt/MT: missing teeth; ft/FT: filled teeth; dmfs/DMFS: decayed missing filled surface index; ds/DS: decayed surfaces; ms/MS: missing surfaces; fs/FS: filled surfaces; CRI: caries restoration index; *: t-test for independent samples; #: chi-square-test according to Pearson

Table 1 Clinical parameters differentiated by Marfan and control group



Figure 1 Example of an arachnodactyly

effective oral hygiene at home more difficult and therefore a higher caries prevalence seems quite understandable. Apart from case reports describing a high incidence of caries [5, 13], there is only one case-control study that has investigated carious lesions in people with Marfan syndrome. In this study, published by De Coster et al. in 2002, 23 people with Marfan syndrome (Marfan group) were examined and compared with 69 randomly selected people (control group) [8]. While there was no significant difference between the Marfan group and the control group when all study participants were examined, the DMFT index in the age group from 0 to 17 years was significantly higher in the Marfan group than in the control group. As a limitation, it must be mentioned here that there was no representative number of cases ($n = 8$) in the Marfan group and that the DMFT index was only presented as a total value and not in its individual components.

The aim of the present study was therefore to investigate the caries experience in children with Marfan syndrome in a larger number of cases and in a detailed manner. The hypothesis formulated was that children and adolescents with Marfan syndrome do not have an in-

creased caries experience compared to a systemically healthy control group with a comparable age structure and gender distribution.

Materials and Methods

The study was approved by the Ethics Committee of the Hannover Medical School (No. 5113). In children of the Marfan group, the diagnosis of classic Marfan syndrome had to be confirmed by molecular genetic examination. The examinations of these children were carried out at the Department of Conservative Dentistry, Periodontology and Preventive Dentistry of the Hannover Medical School as well as at the annual conferences and parent-child seminars of the self-help group “Marfan-Hilfe (Deutschland) e.V.”. The children in the control group were in general medical health and were recruited and examined in a private dental practice. All clinical examinations were performed by a dentist (NW).

The dental examination was performed according to WHO criteria [34]. For this purpose, magnifying glasses, cotton rolls for relative isolation and examination instruments consisting of 2 flat dental mirrors, dental tweezers and a diagnostic probe were used. Examinations, which were carried out at the annual

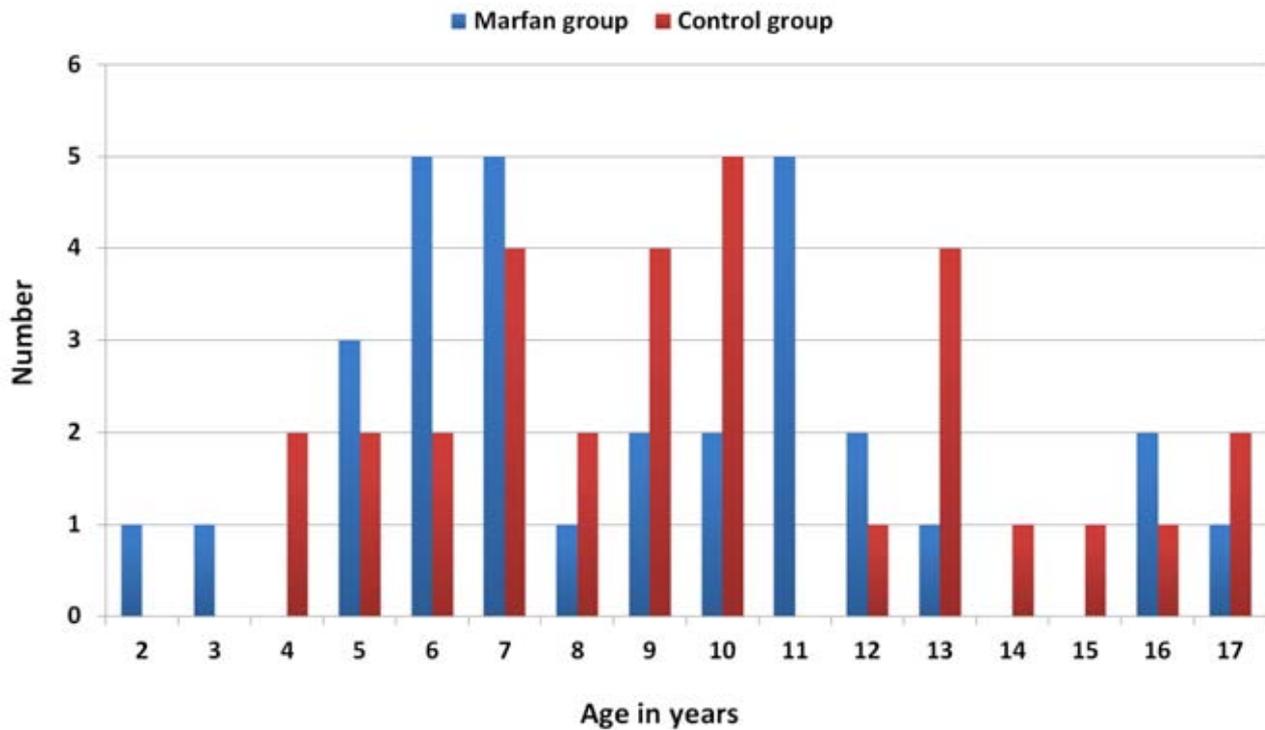
conferences and parent-child seminars of the “Marfan-Hilfe (Deutschland) e.V.”, were performed with the help of a chair with head and neck support and a portable LED lamp. With the help of the dental findings, the dmft and dmfs indices for the teeth of the first dentition and the DMFT and DMFS indices for the teeth of the second dentition (decayed, missing, filled, teeth, surfaces) were calculated in order to assess the dental hard tissue [21]. For further differentiation, the dmft/DMFT and the dmfs/DMFS were subdivided into the individual components dt/DT, mt/MT, ft/FT and ds/DS, ms/MS, fs/FS, respectively. For children and adolescents with a dmft or DMFT > 0 , the caries restoration index (CRI) was calculated using the following formula: CRI (deciduous teeth) = $(mt + ft) / dmft \times 100$ in percent; CRI (permanent teeth) = $(MT + FT) / DMFT \times 100$ in percent [33].

The hygiene index (HI) was used to assess oral hygiene at home [25]. For this purpose, the teeth were stained with a plaque revelator (Mira-2-tone; Hager & Werken GmbH & Co. KG, Duisburg, Germany) and evaluated at 4 measuring points (mesial, buccal, distal and oral). The HI was calculated using the following formula: $\text{sum of plaque-free sites} / \text{sum of all sites} \times 100$ in percent.

Evaluation of the data was performed using the statistics program IBM SPSS Statistics 26 for Windows (IBM, Armonk, NY, USA). For the group comparison (Marfan versus control group), the t-test for independent samples and the chi-square test were used. All tests were bilateral with a significance level of $p \leq 0.05$.

Results

A total of 62 children and adolescents (26 female, 36 male) with an average age of 9.27 ± 3.73 years (minimum: 2 years, maximum: 17 years) were included in the present study. The Marfan group included 31 children with Marfan syndrome (13 female, 18 male, mean age: 8.77 ± 3.72 years), the control group included 31 children in good general medical health (13 female, 18 male, mean age: 9.77 ± 3.72 years). Detailed information on the



Tab. 1, Fig. 1 and 2: A. Rahman and K. Adam

Figure 2 Presentation of the age distribution

age distribution in the Marfan and control group is shown in Figure 2.

The dmft was significantly smaller in the Marfan group than in the control group (0.41 ± 0.59 versus 1.35 ± 1.84 ; $p = 0.040$). The dmfs was also smaller in the Marfan group but did not differ significantly from the control group due to the large standard deviation (0.77 ± 1.15 versus 3.05 ± 4.92 ; $p = 0.056$). A differentiated consideration of the dmft and dmfs indices revealed that the number of filled teeth (ft: 0.18 ± 0.40 versus 1.05 ± 1.73 ; $p = 0.040$) and filled tooth surfaces (fs: 0.36 ± 0.79 versus 2.20 ± 4.10 ; $p = 0.063$) was smaller in the Marfan group than in the control group. The CRI (deciduous teeth) and the number of carious teeth (dt), carious tooth surfaces (ds), missing teeth (mt) and missing tooth surfaces (ms) showed no significant differences between the two groups. Naturally healthy deciduous teeth (dmft = 0) were present in 14 children (63.6%) of the Marfan group and in 10 children (50.0%) of the control group. This difference was not statistically significant. The HI was high in the Marfan group but still significantly lower than in the

control group ($75.36 \pm 16.58\%$ versus $89.44 \pm 8.59\%$; $p < 0.001$).

In the second dentition, the DMFT was smaller in the Marfan group than in the control group (0.52 ± 1.64 versus 1.57 ± 2.46 ; $p = 0.064$). The proportion of filled teeth (FT) was also smaller in the Marfan group than in the control group (0.34 ± 1.05 versus 1.25 ± 2.24 ; $p = 0.059$). In both cases, the difference just missed the level of significance. Naturally healthy permanent teeth (DMFT = 0) were significantly more common in the Marfan group than in the control group (24 versus 15; $p = 0.018$). All other parameters examined showed no significant differences between the two groups (see Table 1).

Discussion

There are case reports in literature that document increased caries in children and adolescents with Marfan syndrome [5, 13]. The only case-control study on caries experience in patients with Marfan syndrome also demonstrated an increased caries risk, particularly in the age group 0 to 17 years [8].

Classical Marfan syndrome is an autosomal-dominant inherited con-

nective tissue disease caused by an FBN1 mutation [23, 26]. Apart from an increased incidence of tooth crowding and the resulting difficulty in oral hygiene, patients with Marfan syndrome do not exhibit any structural features in the area of the tooth crown that promote the development of caries. In a recently published animal study on tooth development, for example, it was shown that FBN1 is not expressed during the development of the crown of the tooth, but only during the development of the root [20]. The hypothesis of the present study was that children and adolescents with Marfan syndrome do not show increased caries experience compared to a systemically healthy control group.

The dmft, dmfs, DMFT, DMFS and the respective individual components of these indices were used to assess caries experience. Representative epidemiological data on caries prevalence in Germany have been published by the Institute of German Dentists (IDZ) and the German Association for Dental Prevention in Children and Adolescents (DAJ) for different age groups [10, 11, 15–17]. In the present study, the children

with deciduous teeth used to calculate dmft, dmfs and the corresponding individual components showed an average age of 6.95 ± 2.36 years (Marfan group) and 7.60 ± 2.09 years (control group). For these values, a comparison with the data from the DAJ (Epidemiologische Begleituntersuchungen zur Gruppenprophylaxe 2009 und 2016), which provide information on the caries prevalence of 6- to 7-year-olds in specific federal states, is useful. The children and adolescents with permanent teeth used to calculate the DMFT, DMFS and the corresponding individual components showed an average age of 9.21 ± 3.44 years in the Marfan group and 10.36 ± 3.42 years in the control group. This data is subsequently compared with those of the Third, Fourth and Fifth German Oral Health Study (DMS III, DMS IV, DMS V), which present the caries experience of 12-year-olds.

In the first dentition, 14 of 22 children with Marfan syndrome (63.6 %) showed naturally healthy dentition. In the control group, this was the case in only 10 of 20 children (50.0 %). The DAJ data show that 53.9 % (2009) and 56.4 % (2016) of the 6 to 7-year-old children had caries-free, naturally healthy deciduous teeth. The dmft was significantly smaller in the Marfan group than in the control group (0.41 ± 0.59 versus 1.35 ± 1.84). A comparable distribution was also observed for the dmfs (0.77 ± 1.15 versus 3.05 ± 4.92). According to the DAJ (2016), the dmft in the 6- to 7-year-old children ranged from 1.37 in Bavaria to 2.31 in Saxony-Anhalt and the nationwide average was 1.73. These values illustrate that both the children in the control group and, in particular, those in the Marfan group showed above-average dmft values. When the individual components were examined, it was found that the ft was significantly smaller in the Marfan group than in the control group (0.18 ± 0.40 versus 1.05 ± 1.73). Neither the dt nor the mt differed significantly between the two groups. According to the DAJ (2016), 6- to 7-year-old children in Germany had an average of 0.74 decayed (dt), 0.19 missing (mt) and

0.80 filled deciduous teeth (ft). A comparison with this data shows that above-average values were available for all individual components in the Marfan Group.

Regarding the second dentition, 82.8% of the children and adolescents in the Marfan group and 53.8% of the children and adolescents in the control group had dentition without caries experience (DMFT = 0). DMS III, IV and V present data from 1997, 2005 and 2014 and show a continuous increase in the proportion of naturally healthy dentition for 12-year-olds (DMS III: 41.8%; DMS IV: 70.1%; DMS V: 81.3%). The mean DMFT was smaller in the Marfan group than in the control group (0.52 ± 1.64 versus 1.57 ± 2.46). However, this difference just missed the significance level. In the DMS III, IV and V, a continuous reduction in caries experience was observed in 12-year-olds with regard to the mean DMFT (DMS III: 1.7; DMS IV: 0.7; DMS V: 0.5) [15–17]. The individual components also showed a positive development in the results of DMS III, IV and V for 12-year-olds. The number of decayed permanent teeth (DT) was reduced from an average of 0.4 (1997) to 0.1 (2014) and the number of filled permanent teeth (FT) from 1.3 (1997) to 0.3 (2014). A comparison with the results of our study shows that the children and adolescents with Marfan syndrome also show values for the individual components (DT: 0.03 ± 0.19 ; MT: 0.14 ± 0.74 ; FT: 0.34 ± 1.05) that correspond to the national average.

Overall, the results of our study show that children and adolescents with Marfan syndrome do not have an increased caries experience. The hypothesis formulated in the introduction was thus confirmed. It should be mentioned at this point that the group sizes are quite small, with a case number of 31, and that further investigations are necessary for representative statements. The reason for the low caries experience in the Marfan group is probably the consistent implementation of suitable prophylactic measures. These consist of a healthy diet, effective biofilm management, targeted fluoride application and regular visits to

the dentist [14, 27]. As a limitation, it must be mentioned that these measures for caries prophylaxis were not included in our study. Another reason for the low caries experience could be the fact that a large part of the families affected by Marfan syndrome participated in activities of the self-help group “Marfan Hilfe (Deutschland) e.V.”. Studies on the topic of self-help have shown that self-help groups make a significant contribution to the personal development and behavioural change of persons with disabilities through the exchange of experience and the provision of information [4]. This leads to a more reasonable utilization of services of the professional care system (the health care system) and an above-average level of cooperation. For the children and young people of the Marfan Group, it can also be assumed that they have received particularly attentive care from their parents with regard to their dental and oral health.

In conclusion, patients with Marfan syndrome have an increased risk of endocarditis and therefore occupy a special position in dental practice. In order to avoid unnecessary dental treatment, the prevention of caries in the first and second dentition plays a decisive role.

Conflict of interest

The authors declare that there is no conflict of interest as defined by the guidelines of the International Committee of Medical Journal Editors.

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